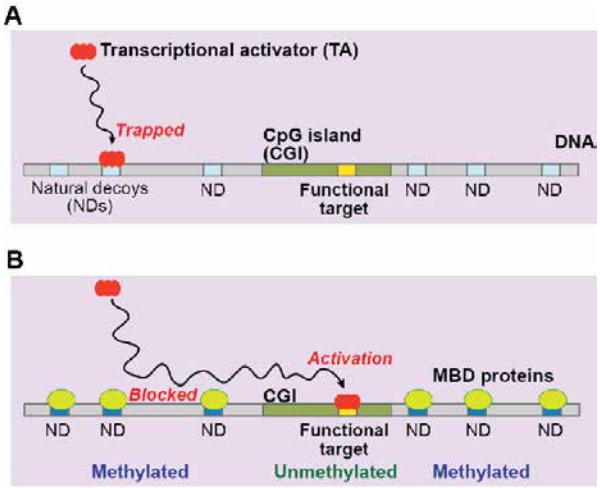
Junji Iwahara, Transcriptomics 2017, 5:2 (Suppl)
DOI: 10.4172/2329-8936-C1-012

DNA methylation as a mechanism that facilitates target search by transcriptional activators

Junji Iwahara
University of Texas Medical Branch, USA

In eukaryotic genomes, there are numerous nonfunctional high-affinity sequences for transcription factors. These sequences potentially serve as natural decoys that sequester transcription factors. We have previously shown that the presence of sequences is like the target sequence could substantially impede association of the transcription factor Egr-1 with its targets. More recently, using a stopped-flow fluorescence method, we examined the kinetic impact of DNA methylation of decoys on the search process of the Egr-1 zinc-finger protein. We analyzed its association with an unmethylated target site on fluorescence-labeled DNA in the presence of competitor DNA duplexes, including Egr-1 decoys. DNA methylation of decoys alone did not affect target search kinetics. In the presence of the MeCP2 methyl-CpG-binding domain (MBD), however, DNA methylation of decoys substantially (~10-20-fold) accelerated the target search process of the Egr-1 zinc-finger protein. This acceleration did not occur when the target was also methylated. These results suggest that when decoys are methylated, MBD proteins can block them and thereby allow Egr-1 to avoid sequestration in nonfunctional locations. This effect may occur in vivo for DNA methylation outside CpG islands and could facilitate localization of some transcriptional activators within regulatory CpG islands, where DNA methylation is rare. Our recent studies to examine this model will be presented.



Biography

Junji Iwahara's current research focuses on the dynamic processes whereby transcription factors scan DNA and recognize their target sites. His group developed some novel methods for investigating the dynamics and kinetics of the protein-DNA interactions at atomic and molecular levels. Using the biophysical and biochemical approaches, his group is trying to better understand how proteins scan and recognize DNA to regulate genes.

j.iwahara@utmb.edu

Notes: